

# Nucleotide and Amino Acid Sequences of Rat HICP

GACGCTTCTG ATCTCCAGAG GACCCTGGGG TGGGACAGGG GCCTTGCCAA GGCTGCAGCC	60
GCTGGGCAGT GGCTTGGAAT GGAGGTCTTT ATTACTGGGA ACTGAGGAGC TAAGAGGCTC	120
CTGTCAGCTT GTCCTAAAGT CTTAGCACTT GTGGTGGCTT GGGCTTCACA CACTGTCAGA	180
CACCTTCGTG GTGGCCTCCA CGGCCTCACC TTCAGGTTTG AAGCTGGCTC CACAAGGGAC	240
ACGGTGAC ATG AGG GGC AGC CCA CTG ATC CAT CTT CTG GCC ACT TCC TTC	290
Met Arg Gly Ser Pro Leu Ile His Leu Leu Ala Thr Ser Phe	
1 5 10	
CTC TGC CTT CTC TCA ATG GTG TGT GCC CAG CTG TGC CGG ACA CCC TGT	338
Leu Cys Leu Leu Ser Met Val Cys Ala Gln Leu Cys Arg Thr Pro Cys	
15 20 25 30	
ACC TGT CCT TGG ACA CCA CCC CAG TGC CCA CAG GGG GTA CCC CTG GTG	386
Thr Cys Pro Trp Thr Pro Pro Gln Cys Pro Gln Gly Val Pro Leu Val	
35 40 45	
CTG GAT GGC TGT GGC TGC TGT AAA GTG TGT GCA CGG AGG CTG GGG GAG	434
Leu Asp Gly Cys Gly Cys Cys Lys Val Cys Ala Arg Arg Leu Gly Glu	
50 55 60	
TCC TGC GAC CAC CTG CAT GTC TGC GAC CCC AGC CAG GGC CTG GTT TGT	482
Ser Cys Asp His Leu His Val Cys Asp Pro Ser Gln Gly Leu Val Cys	
65 70 75	
CAG CCT GGG GCA GGC CCT GGC GGC CAT GGG GCT GTG TGT CTC TTG GAT	530
Gln Pro Gly Ala Gly Pro Gly Gly His Gly Ala Val Cys Leu Leu Asp	
80 85 90	
GAG GAT GAC GGT AGC TGT GAG GTG AAT GGC CGC AGG TAC CTG GAT GGA	578
Glu Asp Asp Gly Ser Cys Glu Val Asn Gly Arg Arg Tyr Leu Asp Gly	
95 100 105 110	
GAG ACC TTT AAA CCC AAT TGC AGG GTC CTG TGC CGC TGT GAT GAC GGT	626
Glu Thr Phe Lys Pro Asn Cys Arg Val Leu Cys Arg Cys Asp Asp Gly	
115 120 125	
GGC TTC ACC TGC CTG CCG CTG TGC AGT GAG GAT GTG CGG CTG CCC AGC	674
Gly Phe Thr Cys Leu Pro Leu Cys Ser Glu Asp Val Arg Leu Pro Ser	
130 135 140	
TGG GAC TGC CCA CGC CCC AAG AGA ATA CAG GTG CCA GGA AAG TGC TGC	722
Trp Asp Cys Pro Arg Pro Lys Arg Ile Gln Val Pro Gly Lys Cys Cys	
145 150 155	
CCC GAG TGG GTA TGT GAC CAG GGA GTG ACA CCG GCG ATC CAG CGC TCC	770
Pro Glu Trp Val Cys Asp Gln Gly Val Thr Pro Ala Ile Gln Arg Ser	
160 165 170	
ACG GCG CAA GGA CAC CAA CTT TCT GCC CTT GTC ACT CCT GCC TCT GCT	818
Thr Ala Gln Gly His Gln Leu Ser Ala Leu Val Thr Pro Ala Ser Ala	
175 180 185 190	
GAT GCT CCT TGT CCA AAT TGG AGC ACA GCC TGG GGC CCC TGC TCA ACC	866

FIGURE 1

1000  
 900  
 800  
 700  
 600  
 500  
 400  
 300  
 200  
 100  
 0

Asp	Ala	Pro	Cys	Pro	Asn	Trp	Ser	Thr	Ala	Trp	Gly	Pro	Cys	Ser	Thr	
				195					200					205		
ACC	TGT	GGG	CTG	GGC	ATA	GCC	ACC	CGA	GTG	TCC	AAC	CAG	AAC	CGA	TTC	914
Thr	Cys	Gly	Leu	Gly	Ile	Ala	Thr	Arg	Val	Ser	Asn	Gln	Asn	Arg	Phe	
			210					215					220			
TGC	CAA	CTG	GAG	ATC	CAA	CGC	CGC	CTG	TGT	CTG	CCC	AGA	CCC	TGC	CTG	962
Cys	Gln	Leu	Glu	Ile	Gln	Arg	Arg	Leu	Cys	Leu	Pro	Arg	Pro	Cys	Leu	
		225					230					235				
GCA	GCC	AGG	AGC	CAC	AGC	TCA	TGG	AAC	AGT	GCT	TTC	TAAGGCCAAC				1008
Ala	Ala	Arg	Ser	His	Ser	Ser	Trp	Asn	Ser	Ala	Phe					
	240					245					250					
TGGGGATGCG	GATACAGGGC	CTGCCATCCT	CAGCAAATGA	CCCTAGGACC	AGGCCCTGGA											1068
CTGCTGGTAG	ATGCTCTTCT	CCATGCTCTT	GGCTGCAGTT	AACTGTCCTG	CTTGGATTCA											1128
CTGTGTAGAG	CCACTGAGCG	ATCCCTGCTC	TGTCTGAGGT	AGGCGGAGCA	GGTGACCAGC											1188
TCCAGTTCTC	TGGTTCAGCC	TGGAATTCTG	GGTTCCTCTG	GCTCATTCCT	CAAAACATCC											1248
CTGTACAAAA	AGGACAACCA	AAAAGACCTT	TAAACCTAGG	CTATACTGGG	CAAACCTGGC											1308
CACCGTGCTG	GGGATAAGGT	CAATGTTAGG	ACCAGACAGC	AGATTGCCTG	AAACTTCCAA											1368
TTCCCTTCTT	GGACTTCTGT	ATGCTTGTCC	CCAAAGATGA	TGAATGAACT	CGTAAGTGTA											1428
CCTTCCCTGA	CCTGAGAACA	CCCTGCCTGC	TCGGGAAGTA	TTCAGGGGCA	GAATTCTCTG											1488
TGAACATGAA	GAGATGAATC	ACACTGTCCT	TAAGAAATTC	CTGAAAGTCC	AGGAACTTGA											1548
GCTTTGTATT	TTCAGGAATG	CACATCTCTT	AAGCACTCGC	AAAACAGGAA	GGCTCCACAC											1608
CTCTGGCAGG	CCAGGGCCTT	TCTCTTCAGC	ATGAGAAAGA	CAAGGGACAG	CAGAGTACTC											1668
TCCTCTGGAG	GACTAGTCTA	GCCTAGAATA	AACACCCAAA													1708

FIGURE 1 (Continued)

**Nucleotide Sequence Encoding Mature HICP and the Amino Acid Sequence of Mature HICP**

CAG CTG TGC CGG ACA CCC TGT ACC TGT CCT TGG ACA CCA CCC CAG TGC	48
Gln Leu Cys Arg Thr Pro Cys Thr Cys Pro Trp Thr Pro Pro Gln Cys	
1 5 10 15	
CCA CAG GGG GTA CCC CTG GTG CTG GAT GGC TGT GGC TGC TGT AAA GTG	96
Pro Gln Gly Val Pro Leu Val Leu Asp Gly Cys Gly Cys Cys Lys Val	
20 25 30	
TGT GCA CGG AGG CTG GGG GAG TCC TGC GAC CAC CTG CAT GTC TGC GAC	144
Cys Ala Arg Arg Leu Gly Glu Ser Cys Asp His Leu His Val Cys Asp	
35 40 45	
CCC AGC CAG GGC CTG GTT TGT CAG CCT GGG GCA GGC CCT GGC GGC CAT	192
Pro Ser Gln Gly Leu Val Cys Gln Pro Gly Ala Gly Pro Gly Gly His	
50 55 60	
GGG GCT GTG TGT CTC TTG GAT GAG GAT GAC GGT AGC TGT GAG GTG AAT	240
Gly Ala Val Cys Leu Leu Asp Glu Asp Asp Gly Ser Cys Glu Val Asn	
65 70 75 80	
GGC CGC AGG TAC CTG GAT GGA GAG ACC TTT AAA CCC AAT TGC AGG GTC	288
Gly Arg Arg Tyr Leu Asp Gly Glu Thr Phe Lys Pro Asn Cys Arg Val	
85 90 95	
CTG TGC CGC TGT GAT GAC GGT GGC TTC ACC TGC CTG CCG CTG TGC AGT	336
Leu Cys Arg Cys Asp Asp Gly Gly Phe Thr Cys Leu Pro Leu Cys Ser	
100 105 110	
GAG GAT GTG CGG CTG CCC AGC TGG GAC TGC CCA CGC CCC AAG AGA ATA	384
Glu Asp Val Arg Leu Pro Ser Trp Asp Cys Pro Arg Pro Lys Arg Ile	
115 120 125	
CAG GTG CCA GGA AAG TGC TGC CCC GAG TGG GTA TGT GAC CAG GGA GTG	432
Gln Val Pro Gly Lys Cys Cys Pro Glu Trp Val Cys Asp Gln Gly Val	
130 135 140	
ACA CCG GCG ATC CAG CGC TCC ACG GCG CAA GGA CAC CAA CTT TCT GCC	480
Thr Pro Ala Ile Gln Arg Ser Thr Ala Gln Gly His Gln Leu Ser Ala	
145 150 155 160	
CTT GTC ACT CCT GCC TCT GCT GAT GCT CCT TGT CCA AAT TGG AGC ACA	528
Leu Val Thr Pro Ala Ser Ala Asp Ala Pro Cys Pro Asn Trp Ser Thr	
165 170 175	
GCC TGG GGC CCC TGC TCA ACC ACC TGT GGG CTG GGC ATA GCC ACC CGA	576
Ala Trp Gly Pro Cys Ser Thr Thr Cys Gly Leu Gly Ile Ala Thr Arg	
180 185 190	
GTG TCC AAC CAG AAC CGA TTC TGC CAA CTG GAG ATC CAA CGC CGC CTG	624
Val Ser Asn Gln Asn Arg Phe Cys Gln Leu Glu Ile Gln Arg Arg Leu	
195 200 205	
TGT CTG CCC AGA CCC TGC CTG GCA GCC AGG AGC CAC AGC TCA TGG AAC	672
Cys Leu Pro Arg Pro Cys Leu Ala Ala Arg Ser His Ser Ser Trp Asn	
210 215 220	

**FIGURE 2**

681

[illegible]

**FIGURE 2 (Continued)**

# Alignment of the Modular Domains of HICP with the Modular Domains of Other

## CCN Family Members

### MODULE I : IGFBP Domain

	28	45	46	60	61	75	76	90	91	100
1	HICP	QLCRTPCT--CP-WTPPQC	-PQGVLVL	DGGCGC	KVCARRLGESCDHLH	VCDPSQGLV	QOPGAG	PGGHGAV	CILL	
2	CTGF	QDCSAQCQ--CAAEAA	PHC	-PAGVSLVL	DGGCGC	RVCAKQ	LGELCTERD	PCDPHKGL	FCDFGSP	ANRKIGVCTA
3	NOV	LRCPSRCPPK	CPSIS-PTC	AP-GVRSVL	DGCSCC	PVCARQ	RQESCS	SEMR	PCDQSSGLY	CDRSAD PNNQTGICMV
4	CYR61	-TCPAACH--CPLEA-PKC	AP-GVGLVR	DGGCGC	KVCAKQLN	EDCSKTQ	PCDHTK	GLECNFGAS	STALKGI	QRA
		* * *	*	*****	**	*	*	**	*	*

### MODULE II : vWFC Domain

	101	120	121	135	136	150	151	165	166	180
1	HICP	DGSC	EVNGRRYLDGETFKP	NCRVLC	RCDGGFTC	LPLCSE	DVRLPSWDC	PRPKRIQ	VF	KGCCPE WVC-----D-Q
2	CTGF	DGAPC	VFGGSVYRSGESFQS	SKYQCT	CLDGAVGC	VPLCSM	DVRLPSPDC	PFPRRV	KLP	KGCKE WVC-----DEP
3	NOV	EGDNC	VFDGVIYRNGEKFEP	NCQYFCT	CRDGGIGC	LPRCQ	LDVLLPGPDC	PAPRK	VAVP	GECCEK WTCGS-----DEQ
4	CYR61	EGRP	PCEYNRIYQNGESFQP	NCKHQCT	CIDGAVGC	IPLCPQ	ELSLPNLGC	PNPRL	VKVS	QCCEE WVCDEDSIKDSLDDQ
		*	*	*	*	*	*	*	*	*

### MODULE III : TSP1 Domain

	240	250	265	280	298	
1	HICP	PCPNWSTAWG	PCSTTCGLGIATRVS	NQNRFCQLEIQRRLC	LPRPCLAA	RSHSSWNSAF-
2	CTGF	NCLVQTTEWS	ACSKTCGMGISTRVT	NDNTFCRLEKQSRLC	MVRPCEAD	LEENIK-KGKK
3	NOV	NCIEQTTEWS	ACSKSCGMGVSTRVT	NRNRQCEMVKQTRLC	IVRPCEQE	PEEVTDKKGGK
4	CYR61	KCIVQTTSWS	QCSKSCGTGISTRVT	NDNPECRLVKETRIC	EVRPCGQ	PVYSSLK-KGKK
		*	*	*	*	*

FIGURE 3

Northern Blot Analysis of HICP Expression in Rat Aorta Smooth Muscle Cells

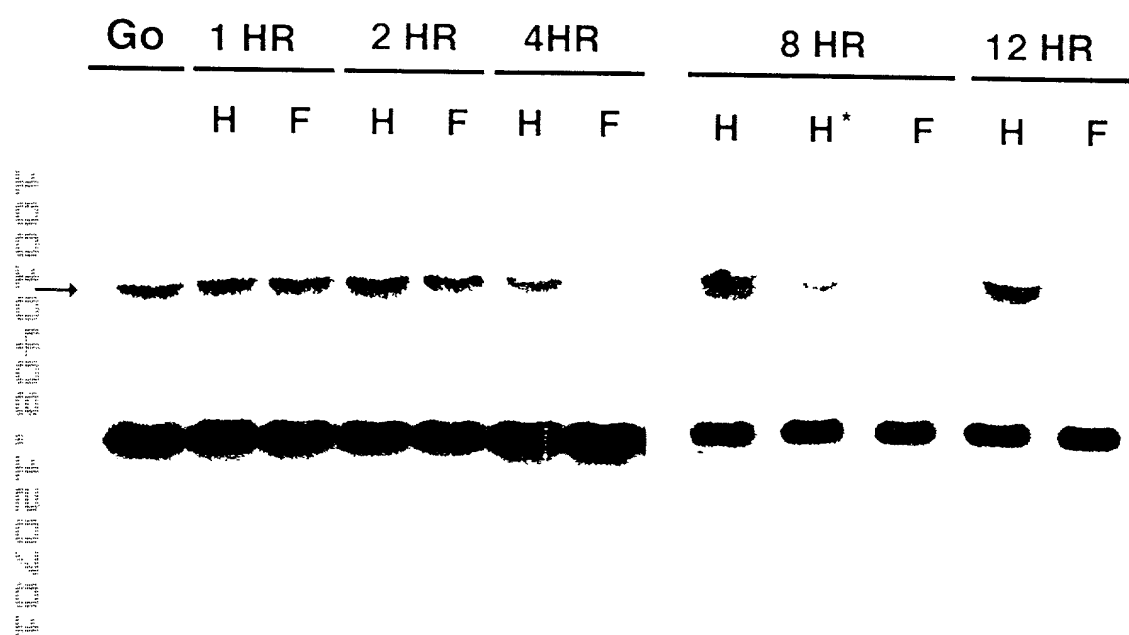


FIGURE 4

## DNA Synthesis in Rat Aorta Smooth Muscle Cells

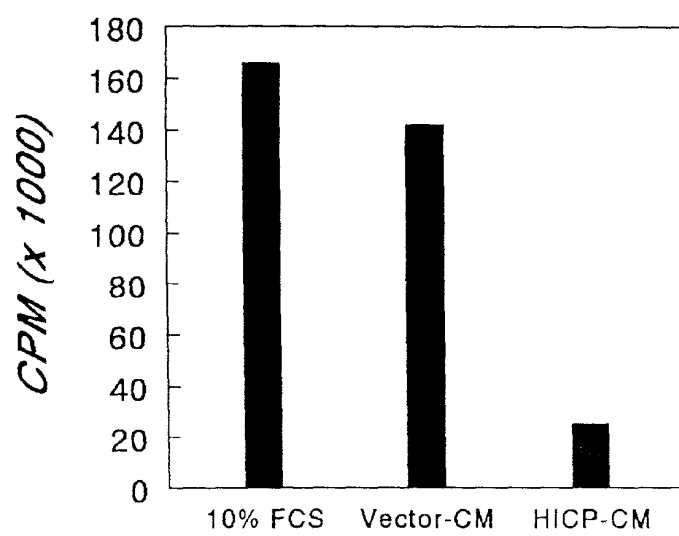


FIGURE 5